Steric Effect in Regioselective Cyclization of 3,4-Epoxy Alcohols to Oxetanes[1)]

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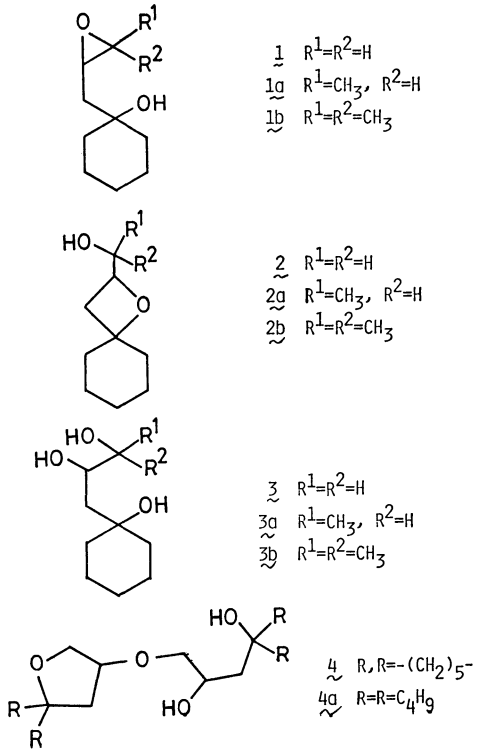
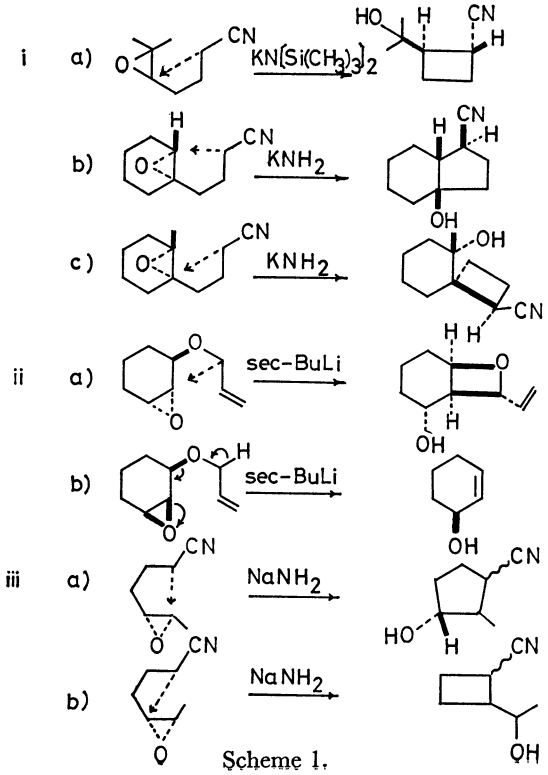
(Received December 3, 1979)

A number of 3,4-epoxy alcohols, involving critical structural factors for oxetane formation by intramolecular cyclization, were prepared and treated with base under aqueous (KOH in 75% aq DMSO) and anhydrous conditions (NaH in THF). The result of the reactions of *cis*- and *trans*-4,5-epoxy-2-methyl-2-undecanols, coupled with that of 1-(2,3-epoxybutyl)- and 1-(2,3-epoxy-3-methylbutyl)-1-cyclohexanols (**1a** and **1b**), indicated that the regioselective oxetane formations of 3,4-epoxy alcohols with alkoxide anions are much insensitive to steric hindrance at the attacked oxirane rings, compared with the corresponding reactions with carbanions, while that of 1-(2,3-epoxypropyl)-1-cycloalkanols revealed that the relevant reactions depend on bulkiness of attacking alkoxide anions. Moreover, the result of the reactions of 1-(1,2-epoxycycloalkyl)-2-methyl-2-propanols under the aqueous conditions demonstrated that the oxetane formations are affected seriously by steric hindrance at the attacked oxirane rings, although the result was in striking contrast with the corresponding result with carbanions. On the other hand, the reactions of 3,4-epoxy alcohols under the anhydrous conditions proceeded in different manner, depending on the structures of the epoxides; namely, fragmentation took place as major reactions with some epoxides, while intramolecular cyclization occurred predominantly with other epoxides.

In previous papers[2a)] we reported that treatment of 1-(2,3-epoxypropyl)-1-cyclohexanol (**1**) and its methyl analogues with base in 75% aqueous dimethyl sulfoxide (DMSO) produced the corresponding four-membered ether (oxetane) (**2**) and its methyl analogues as the sole cyclized products other than hydrolysis products (**3**), while the treatment under anhydrous conditions in aprotic solvents led to formation of a dimeric five-membered ether (oxolane) (**4**) or of a simple alcoholysis product.[2b)] The regioselective formation of oxetanes was rationalized[2b)] mainly in terms of "collinearity requirement," which was proposed first by Stork and coworkers[3)] on the basis of the regioselective cyclization of 4,5-epoxy nitriles to cyclobutanes (Scheme 1, i-a), and accentuated later by Still[4)] from intramolecular cyclization of allyl 2,3-epoxyalkyl ether to a four-membered ring (oxetane) (Scheme 1, ii-a). However, Lallemand and Onanga[5)] criticized their explanation from the result of preferential cyclizations of "non-rigid" *trans*- and *cis*-3,4-epoxy nitriles to cyclopentanes and cyclobutanes, respectively, (Scheme 1, iii, *cf.*, i-b and i-c) and emphasized the importance of "steric hindrance" at the oxirane rings towards the attack of carbanions rather than the "requirement." Moreover, Stork and coworkers[3)] pointed out the effect of "bond distortion" as one of the factors which control the "requirement" on the basis of the result of the cyclizations of 4,5-epoxy nitriles. These apparently inconsistent facts on steric factors concerning the oxirane



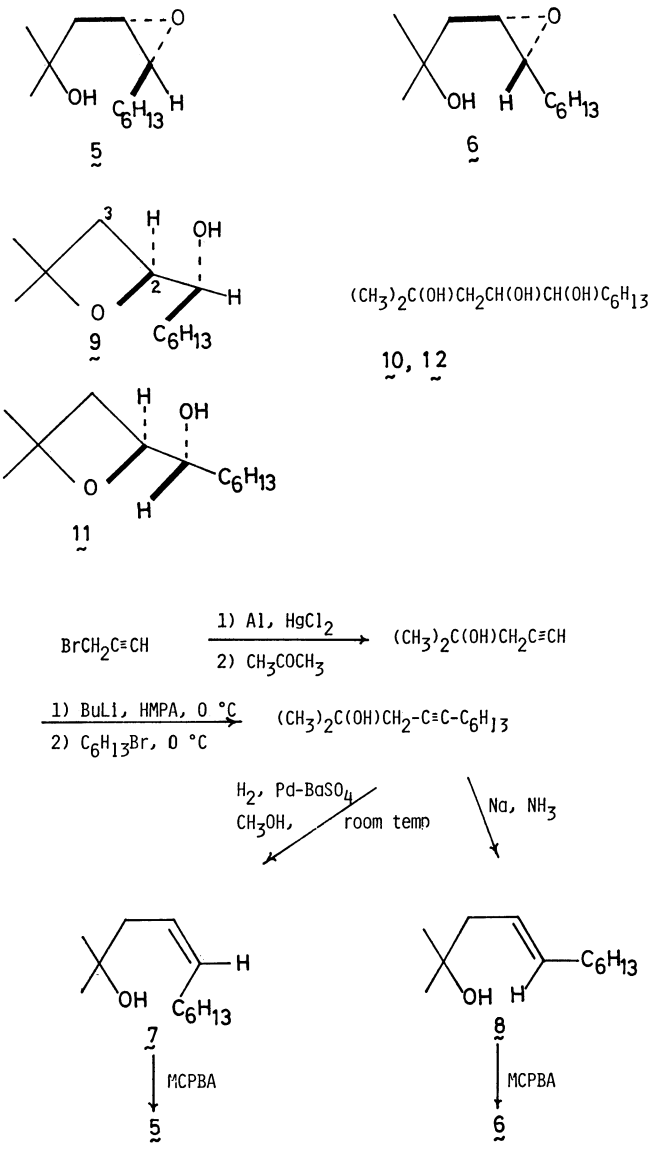


Scheme 1.

ring cleavage[6] prompted us to investigate the reactions of 3,4-epoxy alcohols, whose structures are closely related to the geometrical features of the above reactions, with base under the aqueous conditions. The results corroborating the relevant regioselectivity have recently been reported in preliminary form,[7] and the details are described in the present paper with additional results on the reactions carried out under anhydrous conditions.

Aqueous Conditions. I. Non-fused System.[8] *cis*- and *trans*-4,5-Epoxy-2-methyl-2-undecanols (**5** and **6**) were prepared by epoxidation[9] of the corresponding alkenols, *cis*- and *trans*-2-methyl-4-undecen-2-ols (**7** and **8**), as depicted in Scheme 2. These epoxy alcohols (**5** and **6**), corresponding to Lallemand's *cis*- and *trans*-4,5-epoxy nitriles (Scheme 1, iii), were submitted to base treatment under the controlled conditions [10 equiv KOH in 75% aq DMSO, 105—110 °C (bath temp), 2 h].[10] The reaction of *cis*-epoxide (**5**) proceeded as expected to give the corresponding oxetane (**9**) and hydrolysis product (triol) (**10**) in 40 and 30% yields with the recovered epoxide (**5**, 15%). In accordance with the assigned oxetane structure, compound **9** exhibited a strong absorption at 964 cm^{-1} in the IR spectrum and displayed signals due to protons at C-3 and C-2 on the oxetane (not oxolane) ring at δ 2.18 (2H, d, J=8 Hz) and 4.40 (1H, dt, J=5 and 8 Hz) in the NMR spectrum. These spectral patterns were characteristic of oxetanes, as had been demonstrated previously.[2] The same reaction of *trans*-epoxide **6** gave almost the same result; namely, the corresponding oxetane (**11**) and triol (**12**) were isolated in 50 and 19% yields, respectively, with the recovered epoxide (**6**, 8%). The structure of oxetane **11** was also clarified by the spectral data: IR, 984 and 960 cm^{-1}; NMR, δ 2.10 and 2.30 (each 1H, dAB_q, J=12 and 8 Hz, 3-H) and 4.53 (1H, dt, J=4 and 8 Hz, 2-H). The reaction result, in contrast with the Lallemand result (preferential cyclopentane formation from the *trans*-epoxy nitriles),[5] indicates that the intramolecular reactions of non-rigid 3,4-epoxy alcohols with alkoxide anions in 75% aqueous DMSO are much insensitive to steric hindrance at the attacked oxirane, compared with those with carbanions.

In connection with this, we treated 1-(2,3-epoxybutyl)-1-cyclohexanol[2] (**1a**) and its 3-methyl analogue (**1b**) with base under almost the same aqueous conditions. The latter epoxide (**1b**) could be prepared by epoxidation of the corresponding olefin[2a] with *m*-chloroperbenzoic acid (MCPBA) in an alkaline "biphasic" solvent system[11] in a 91% yield, although the compound (**1b**) was very sensitive to acid and converted readily into the corresponding oxolane, as had been described previously.[2a] Interestingly, both the epoxy alcohols (**1a** and **1b**) gave the corresponding oxetanes (**2a** and **2b**) in practically the same yields (73 and 72%) along with the simple hydrolysis products (**3a** and **3b**) (9 and 8%). This result indicates that yields of the oxetanes formed do not always increase with the number of substituents on the oxirane ring, supporting the aforementioned insensitivity to steric hindrance at the attacked oxirane rings in the oxetane formation.



Scheme 2.

Moreover, the fact that these oxetanes (**2a** and **2b**) were formed in better yields (73%) than oxetanes **9** and **11** (40 and 50%) led us to have interest in examining the effect of the bulkiness of the attacking alkoxide anions in the relevant cyclization.

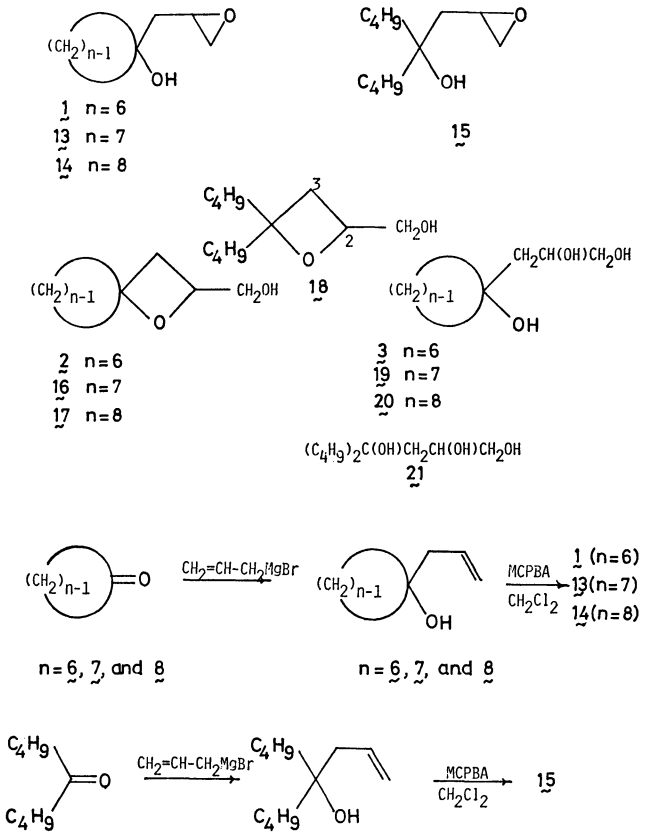
Four 1-(2,3-epoxypropyl)-1-cycloalkanols (**1**, **13**—**15**), differing only in bulkiness of the attacking anions, were used for the examination; namely, the cyclohexanol[2] (**1**), cycloheptanol (**13**), cyclooctanol (**14**), and 4-butyl-1,2-epoxy-4-octanol (**15**) were prepared from the corresponding olefins as described in Scheme 3 and treated with base under the relevant aqueous conditions. The result is summarized in Table 1. The structures of these products were deduced mainly from the spectral data, as exemplified by those of oxetane **18**, which showed a strong absorption at 965 cm^{-1} in the IR spectrum and exhibited a two-proton doublet (J=8 Hz) at δ 2.21 and one proton multiplet at δ 4.60 due to protons at C-3 and C-2 on the oxetane ring, respectively, and also two double doublets (each 1H, dAB_q, J=12, 5 and 12, 3.5 Hz) due to two hydroxymethyl

Table 1. Reactions of 1-(2,3-epoxypropyl)-1-cycloalkanols (**1**, **13**—**15**) with base under aqueous conditions[a)]

Compound	Temp/°C	Time/min	Oxetane[b)]	Triol[b)]
1	135	90	**2**(49)	**3**(32)
13	135	90	**16**(25)	**19**(55)
14	80	100	**17**(20)	**20**(60)
15	65	100	**18**(20)	**21**(60)

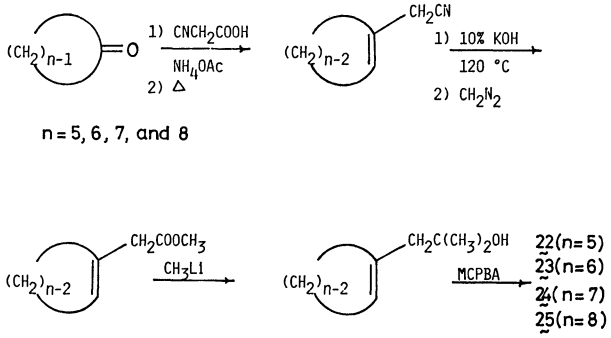
a) Ten equiv KOH in 75% aq DMSO. b) The figures in parentheses denote "isolated yields."

protons at δ 3.54 and 3.68, respectively. As shown in Table 1, only the corresponding oxetanes and triols were isolated in all the cases. However, the yield of oxetanes decreased in the order of increasing ring size. The result, coupled with the aforementioned one (**1a** and **2a**), implies that the increasing bulkiness of attacking alkoxide anions considerably suppresses the intramolecular reaction (oxetane formation) rather than the intermolecular (hydrolysis).



Scheme 3.

Aqueous Conditions. II. Fused System.[8)] Four 1-(1,2-epoxycycloalkyl)-2-methyl-2-propanols (**22**—**25**), were prepared from cycloalkanones *via* six-step processes as described in Scheme 4. These 3,4-epoxy alcohols, in each of which an oxirane ring is fused with a cycloalkane ring, correspond to Stork's fused 4,5-epoxy nitriles[3)] (Scheme 1, i-b). Treatment of the compounds with base under almost the same aqueous conditions produced multi-component mixtures, which were separated by preparative TLC, respectively. The structure and yield of identified products are summarized in Table 2. A typical example of the structure elucidation is illustrated by the oxolane (**29**) in the Table. The MS [*m/e* 170 (M^+), 155, and 137], IR [3600, 3420, 1150, and 1035 cm^{-1}], and NMR spectra [δ 1.35 (6H, s, $2CH_3$), 1.84 and 1.94 (each 1H, d, J=13 Hz, 3-H)] were consistent with the assigned structure. The relevant bridge-head proton on the carbon (C-7a) adjacent to the oxolane oxygen atom was observed at δ 3.79 as a triplet with J=4 Hz. The coupling constant indicates that the oxolane C-7a–O bond is oriented axial and

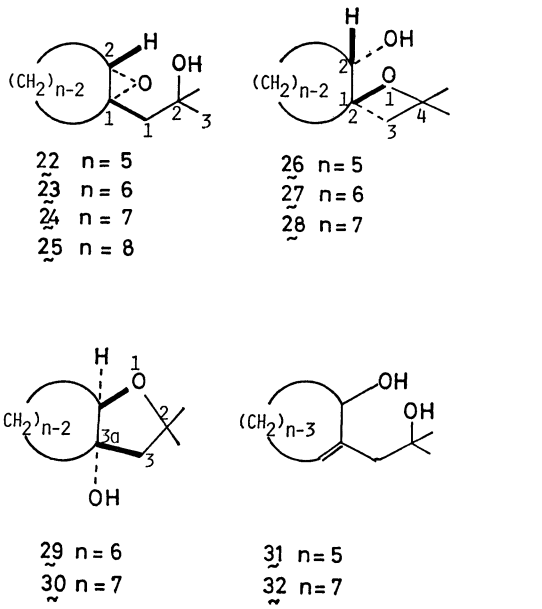


Scheme 4.

Table 2. Reactions of 1-(1,2-epoxycycloalkyl)-2-methyl-2-propanols (**22**—**25**) with base under aqueous conditions[a)]

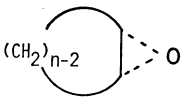
Compound	Temp/°C	Time/min	Products[b)]			
			Oxetane	Oxolane	Triol	Diol
22	135	90	**26**(35)	—	(17)	**31**(8)
23	140	90	**27**(46)	**29**(7)	(12)	—
24	115	110	**28**(24)	**30**(22)	—	**32**(9)
25	140	150	—	—	—	—

a) Ten equiv KOH in 75% aq DMSO. b) The figures in parentheses denote "isolated yields."

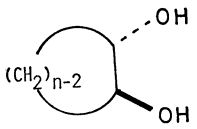


hence the oxolane C-3a–C-3 bond must be equatorial in respect to the cyclohexane ring. This assignment demonstrates that the oxolane (**29**) was formed by attack of the alkoxide anion to the oxirane ring from the back side.[6c,12] The configurations of all products in Table 2 were assigned on the basis of the spectral data and the back-side attack.

As shown in Table 2, the cyclopentene and cyclohexene oxides (**22** and **23**) afforded the corresponding oxetanes (**26** and **27**) as the sole and major cyclized products, respectively. However, the cycloheptene oxide (**24**) gave both the corresponding oxetane and oxolane (**28** and **30**) in almost the same yields, while the cyclooctene oxide (**25**) underwent no oxirane ring cleavage. In connection with this, simple (unsubstituted) cycloalkene oxides (**33**—**36**) were treated under almost the same conditions [10 equiv KOH in 75% aq DMSO, 100—110 °C (bath temp)]. While cyclohexene oxide



33 n = 6
34 n = 7
35 n = 8
36 n = 12

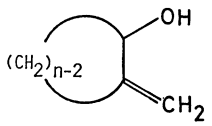


37 n = 6
38 n = 7

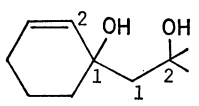
(**33**) was hydrolyzed rapidly to yield cyclohexane-1,2-diol (**37**) (100% within 0.5 h), cycloheptene oxide (**34**) reacted relatively slowly giving the corresponding diol (**38**) in 70 and 80% yields after 0.5 and 3 h, respectively. On the other hand, cyclooctene and cyclododecene oxides (**35** and **36**) were recovered unchanged almost quantitatively after 3 h treatment. The reactivity in the hydrolysis of these simple cycloalkene oxides clearly reflects steric hindrance against the back-side attack of hydroxide anions to the oxirane carbon atoms. Examination of the Dreiding model reveals that the hindrance also make it difficult to achieve the "collinear arrangement" for the intramolecular cyclization leading to formation of oxetane rather than that of oxolane. The result of the reactions of compounds **24** and **25** with fused medium-sized cycloalkane rings illustrates oxetane formation which is affected seriously by the "steric hindrance" under the relevant aqueous conditions. Nevertheless, the result shown in Table 2 is in striking contrast with the Stork's result. In summary, the oxetane formation from 3,4-epoxy alcohols, apart from the compounds with the afore-mentioned exceptional structural features (*e.g.*, compounds **24** and **25**), under the aqueous conditions proceeds regioselectively and would be rationalized mostly in terms of the "collinearity requirement" in the transition state, though it obviously depends on "steric effect" to some extent.

Anhydrous Conditions. Two non-fused compounds **1b** and **15** and three fused compounds **23**, **24**, and **25** were examined under anhydrous conditions. Compound **15**, when treated with sodium hydride (NaH) in tetrahydrofuran (THF) under reflux, gave the corresponding dimeric oxolane (**4a**) in a 60% yield as expected from the result of the reactions of related compounds.[2a] However, the same treatment of **1b** produced the corresponding oxetane (**2b**) in a 30% yield as a sole cyclized product, leaving a considerable amount (57%) of the starting epoxide (**1b**) unchanged. The fact offers the first example indicating importance of the steric hindrance in oxirane ring opening in anhydrous aprotic solvents. This apparently unexpected result, which is also inconsistent with "Thorpe-Ingold effect,"[13] seems to be in line with our previous rationalization proposed for the solvent dependency in ring closure;[2a] namely, "the cyclization in question in anhydrous aprotic solvents would proceed with displacement at the less-substituted carbon of the oxirane ring, leading to formation of oxygen heterocycles with less steric constraint." However, for want of other examples, we do not prefer to make further mechanistic discussion.

Treatment of the fused compounds (**23**—**25**) with base under almost the same anhydrous conditions resulted in fragmentation as the respective main reactions. The cyclohexene oxide (**23**), when treated with NaH in refluxing THF, gave a complex mixture, from which 2-methylenecyclohexanol (**39**) was isolated as a major product (38%) along with the corresponding oxetane (**27**) (27%) and 1-(2-hydroxy-2-methylpropyl)-2-cyclohexene-1-ol (**40**) (9%) by preparative TLC. The same treatment of the cycloheptene and cyclooctene oxides (**24** and **25**) afforded the corresponding 2-methylenecycloalkanols (**41** and **42**) in 55 and 18% yields, respectively, with recovery of the starting epoxides (**24** and **25**, 9 and 52%), no other compounds being detected. Formation of these 2-methylenecycloalkanols (**39**, **41**, and **42**) and cyclohexenol (**40**) might



39 n = 6
41 n = 7
42 n = 8



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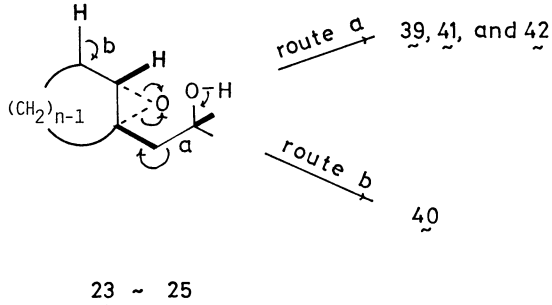
be understood as results of usual fragmentation reactions, route a (*cf.*, Scheme 1, ii-b) and route b, as shown in Scheme 5, indicating the special character of 75% aqueous DMSO as a solvent system. However, the



Scheme 5.

reason why the fragmentation occurred predominantly with the fused epoxy alcohols and that why the oxetane (**27**) was formed in preference to the corresponding oxolane (**29**), were explained only with difficulty. In view of the remarkable contrast of the results between the aqueous and anhydrous conditions as well as between the non-fused and fused compounds, we only emphasize that the present results provide intrinsic problems for the mechanistic studies involving steric factors, solvent effects, and others.

Experimental

All the melting and boiling points were uncorrected. The homogeneity of each compound was always checked by TLC over silica gel (Wakogel B-5F) with various solvent systems, and the spots were developed with cerium(IV) sulfate in dil sulfuric acid. The IR and NMR (100 MHz) spectra were measured in liquid state and in chloroform-*d*, respectively, unless otherwise stated. The abbreviations "s, d, t, m, and br" in the NMR spectra denote "singlet, doublet, triplet, multiplet, and broad," respectively. The preparative TLC and column chromatography were carried out over silica gel (Wakogel B-5F) and silicic acid (Merck, Kieselgel 60, 70—230 mesh), respectively. The following solvents were distilled before use after being dried; ether and THF from lithium aluminium hydride (LAH); dichloromethane from phosphorus pentaoxide; DMSO and hexamethylphosphoramide (HMPA) from calcium hydride. The latter two solvents were stored over Molecular Sieve.

*Preparation of 1-(2,3-Epoxy-3-methylbutyl)-1-cyclohexanol (**1b**).* A mixture of 1-(3-methyl-2-butenyl)-1-cyclohexanol[2a] (116 mg) in dichloromethane (5 ml) and 0.5 M aq sodium hydrogencarbonate ($NaHCO_3$, 4 ml) (pH 8.3) was stirred with MCPBA (173 mg, purity 90%) at 0 °C for 30 min.[9] The mixture was washed with 5% aq sodium thiosulfate ($Na_2S_2O_3$), 5% aq $NaHCO_3$ and water, dried and evaporated to leave **1b** (119 mg), oily; MS, *m/e* 184 (M^+) and 166; IR ($CHCl_3$), 3620, 3460, 1110, 1035, 1010, and 910 cm^{-1}; NMR, δ 1.29 and 1.35 (each 3H, s, CH_3 at C-3), and 3.04 (1H, dd, J=5 and 8 Hz, 2-H). The oil was used for the next reaction without further purification.

Preparation of cis- *and* trans-*4,5-Epoxy-2-methyl-2-undecanols (**5** and **6**). i)*: To a solution of 2-methyl-4-pentyn-2-ol[14] (3.0 g, 0.03 mol) in dry HMPA (80 ml) cooled with an ice–water bath was added 15% butyllithium in hexane (40 ml) under stirring. The mixture was stirred at 0 °C for 40 min and then warmed at *ca.* 25 °C under reduced pressure, when the hexane had been removed. To the residue was added freshly distilled hexyl bromide (8 g, 0.048 mol) dropwise at 0 °C, and the mixture was stirred at 0—15 °C for 18 h and at 40—50 °C for 1 h, and cooled.[15] The reaction mixture was mixed with water (50 ml) and extracted with ether (4×50 ml). The ether solution was washed with water and with saturated brine, dried and evaporated to leave an oily substance (4.0 g), which was purified by passing through a silica gel column to yield 2-methyl-4-undecyn-2-ol; bp 113—117 °C (bath temp) (17 Torr); MS, *m/e* 182 (M^+) and 167; IR, 3380, 1148, 1125, and 980 cm^{-1}; NMR, δ 0.90 (3H, br t, J=6 Hz, 11-H), 1.28 (6H, s, CH_3 at C-2 and 1-H), 2.04 (1H, s, OH), 2.20 (2H, m, 6-H), and 2.35 (2H, t, J=2 Hz, 3-H).

The alkynic alcohol (300 mg) was hydrogenated over Lindlar catalyst (500 mg) in methanol at room temperature for 1 h under stirring. After removal of the catalyst, the mixture was evaporated to give *cis*-2-methyl-4-undecen-2-ol (**7**, 290 mg), showing a single spot on TLC, bp 83—86 °C (bath temp) (17 Torr); MS, *m/e* 169 (M^+-CH_3) and 166 (M^+-H_2O); IR, 3380, 905, and 790 cm^{-1}; NMR, δ 1.89 (3H, br t, J=6 Hz, 11-H), 1.24 (6H, s, CH_3 at C-2 and 1-H), 2.10 (2H, m, 6-H), 2.29 (2H, d, J=6 Hz, 3-H), 5.51 and 5.63 (each 1H, dt, J=11 and 6 Hz, 5- and 4-H).

To a solution of **7** (240 mg, 1.3 mmol) in dry dichloromethane (10 ml) cooled with an ice–water bath was added MCPBA (0.51 g, 1.9 mmol), and the mixture was stirred at 0 °C for 15 min and then allowed to stand in a refrigerator for 15 h. The reaction mixture was washed with 5% aq $Na_2S_2O_3$ and then with 5% aq sodium carbonate (Na_2CO_3), and extracted with dichloromethane (3×20 ml). The dichloromethane solution was worked up as usual to leave oily residue, which was purified by chromatography over silica gel to give **5** (204 mg), bp 108—110 °C (14 Torr); MS, *m/e* 200 (M^+), 185, 167, 127, and 86 (base); IR, 3420 and 1240 cm^{-1}; NMR, δ 0.90 (3H, br t, J=6 Hz, 11-H), 1.33 and 1.36 (each 3H, s, CH_3 at C-2 and 1-H), 2.96 (1H, m, 5-H), and 3.20 (1H, dt, J=4 and 9 Hz, 4-H). Found: C, 71.55; H, 11.96%. Calcd for $C_{12}H_{14}O_2$: C, 71.95; H, 12.08%.

ii): To liquid ammonia (6 ml), distilled from sodium, containing sodium (207 mg, 9 mmol) was added the aforementioned alkynic alcohol (360 mg, 2 mmol) in dry ether, and the mixture was stirred under reflux for 2 h. After additions of ammonium chloride (2 g) and then of aq ammonia (5 ml), the reaction mixture was evaporated and extracted with ether (3×30 ml). The ether solution was washed with dil hydrochloric acid (HCl) and water, dried and evaporated to give *trans*-2-methyl-4-undence-2-ol (**8**, 230 mg), showing a single spot on TLC, bp 102—105 °C (bath temp) (17 Torr); MS, *m/e* 169 (M^+-CH_3) and 166 (M^+-H_2O); IR, 3380 and 968 cm^{-1}; NMR, δ 0.85 (3H, br t, J=6 Hz, 11-H), 1.16 (6H, s, CH_3 at C-2 and 1-H), 2.16 (4H, br m, 3- and 6-H), and 5.48 (2H, m, 4- and 5-H).

Compound **8** (150 mg) was epoxidized with MCPBA (0.40 g) in dichloromethane (10 ml) in the same manner as described above to yield **6** (110 mg), bp 126—130 °C (bath temp) (17 Torr); MS, *m/e* 200 (M^+), 185, 127, and 86 (base); IR, 3420 and 1240 cm^{-1}; NMR, δ 0.86 (3H, br t, J=6 Hz, 11-H), 1.28 and 1.31 (each 3H, s, CH_3 at C-2 and 1-H), 2.70 and 2.90 (each 1H, m, 5- and 4-H). Found: C, 71.57; H, 11.97%. Calcd for $C_{12}H_{24}O_2$: C, 71.95; H, 12.08%.

*Reaction of **5** and **6** under Aqueous Conditions. i)*: A solution of **5** (150 mg, 0.75 mmol) in DMSO (22.5 ml) and water (7.5 ml) was heated gradually from 50 °C to 115 °C (bath temp) for 2 h (at 50 °C for 0.5 h, at 80 °C for 0.5 h, at 95 °C for 0.5 h and then at 115 °C for 0.5 h), with potassium hydroxide (KOH, 520 mg, 9.3 mmol) under nitrogen with stirring, when the spot of **5** had disappeared on TLC. The reaction mixture was cooled, poured into saturated brine, and extracted with ethyl acetate (5×30 ml). The organic solution was washed with saturated brine, dried and evaporated to leave an oily residue, which was separated by chromatography over silica gel (10 g), benzene–ethyl ether mixtures being used as solvents. Fractions eluted with benzene–ether (10 : 1) gave *threo*-2-(1-hydroxyheptyl)-4,4-dimethyloxetane (**9**, 58 mg), bp 85—87 °C (bath temp) (15 Torr); MS, *m/e* 185 (M^+-CH_3) and 115; IR, 3440, 964, 940, and 910 cm^{-1}; NMR, δ 0.85 [3H, br t, J=5 Hz, $(CH_2)_5CH_3$], 1.35 and 1.47 (each 3H, s, CH_3 at C-4), 2.18 (2H, d, J=8 Hz, 3-H), 3.54 [1H, t, J=5 Hz, CH(OH)], and 4.40 (1H, dt, 5 and 8 Hz, 2-H). Found: C, 71.99; H, 12.11%. Calcd for $C_{12}H_{24}O_2$: C, 71.95; H, 12.08%. Later fractions eluted with benzene–ether (1: 1) afforded 2-methylundecane-2,4,5-triol (**10**, 64 mg), amorphous; MS, *m/e* 203 (M^+-CH_3) and 200; IR, 3380 cm^{-1}; NMR, δ 0.89 (3H, br t, J=6 Hz, 11-H), 1.28 and 1.33 (each 3H, s, CH_3 at C-2 and 1-H), 1.49 and 1.80 (each 1H, dd, J=

14, 2.5 and 14, 10 Hz, 3-H), 3.39 and 3.84 (each 1H, m, 5- and 4-H). Found: C, 65.88; H, 12.01%. Calcd for $C_{13}H_{26}O_3$: C, 66.01; H, 12.00%.

ii): Compound **6** (100 mg, 0.5 mmol) was treated with KOH (360 mg, 6 mmol) in DMSO (15 ml) and water (5 ml) in the same manner as **5**. The reaction mixture was worked up and purified as mentioned above to give *erythro*-oxetane (**11**, 50 mg), a diastereoisomer of **9**, and triol (**12**, 21 mg), which showed the following spectra. **11**, bp 106—108 °C (bath temp) (15 Torr); Ms, *m/e* 200 (M^+) and 185; IR, 3430, 984, and 960 cm^{-1}; NMR, 0.86 [3H, br t, J=6 Hz, $(CH_2)_5$-CH_3], 1.35 and 1.49 (each 3H, s, CH_3 at C-4), 2.10 and 2.30 (each 1H, dAB_q, J=12 and 8 Hz, 3-H), 3.69 [1H, m, CH(OH)] and 4.53 (1H, dt, J=4 and 8 Hz, 2-H). Found: C, 71.96; H, 12.09%. Calcd for $C_{12}H_{24}O_2$: C, 71.95; H, 12.08%. **12**, mp 50—53 °C (from ether–hexane); MS, 203 ($M^+ - CH_3$) and 200 ($M^+ - H_2O$); IR (Nujol), 3260 cm^{-1}; NMR, δ 0.88 (3H, br t, J=6 Hz, 11-H), 1.29 (6H, s, CH_3 at C-2 and 1-H), 1.76 (1H, dAB_q, J=10 and 14 Hz, one of 3-H), 3.61 (1H, m, 5-H), and 3.93 (1H, ddd, J=14, 6, and 2 Hz, 4-H). Found: C, 66.42; H, 11.82%. Calcd for $C_{12}H_{26}O_3$: C, 66.01; H, 12.00%.

Preparation of 1-(2,3-Epoxypropyl)-1-cycloheptanol (13), 1-(2,3-Epoxypropyl)-1-cyclooctanol (14), and 1,2-Epoxy-4-butyl-4-octanol (15). *i)*: A solution of freshly distilled cycloheptanone (1.12 g, 0.01 mol) in ether (10 ml) was added dropwise to a cold suspension of allylmagnesium bromide, prepared from allyl bromide (2.44 g) and magnesium (0.5 g), activated by heating, in ether (16 ml), and the whole mixture was stirred at room temperature for 13.5 h.[16] After dropwise addition of dil aq ammonia (7 ml), the reaction mixture was extracted with ether (4×10 ml). The ether solution was worked up as usal to leave an oily residue, which was distilled fractionally under reduced pressure to give 1-allyl-1-cycloheptanol (1.12 g), bp 85—88 °C (11 Torr); MS, *m/e* 154 (M^+) and 136; IR, 3380, 3060, 1640, and 905 cm^{-1}; NMR, δ 2.22 (2H, d, J= 8 Hz, CH_2=CHCH_2), 5.04 and 5.12 (each 1H, dd, J=4, 17 and 4, 10 Hz, CH_2=CHCH_2), and 5.80 (1H, ddt, J=17, 10, and 8 Hz, CH_2=CHCH_2). Found: C, 77.66; H, 11.75%. Calcd for $C_{10}H_{18}O$: C, 77.86; H, 11.76%.

The allyl cycloheptanol (1.01 g, 6.60 mmol) in dichloromethane (35 ml) was epoxidized with MCPBA (2.26 g) at room temperature under stirring in a usual manner. The reaction mixture was worked up as usual and purified by chromatography over silica gel (35 g) to give **13** (985 mg), bp 83—85 °C (15 Torr); MS, *m/e* 170 (M^+) and 152; IR, 3440 and 1250 cm^{-1}; NMR, δ 1.89 [2H, d, J=7 Hz, CH_2CH-(-O-)CH_2], 2.05 and 2.77 [each 1H, dd, J=5, 2 and 5, 5 Hz, CH_2CH(-O-)CH_2], and 3.13 [1H, m, CH_2CH(-O-)CH_2]. Found: C, 70.32; H, 10.54%. Calcd for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66%.

ii): 1-Allyl-1-cyclooctanol (2.35 g) was prepared by treatment (room temp, 17 h) of cyclooctanone (2.27 g, 0.018 mol) with allylmagnesium bromide, prepared from allyl bromide (4.36 g, 0.036 mol) and magnesium turnings (0.9 g, 0.036 mol) in ether (50 ml), followed by fractional distillation, and had the following properties: bp, 99—101 °C (12 Torr); MS, *m/e* 168 (M^+) and 150; IR, 3400, 3070, 1640, and 910 cm^{-1}; NMR, δ 2.20 (2H, d, J=8 Hz, CH_2CH=CH_2), 5.07 and 5.11 (each 1H, dd, J=17, 1 and 10, 1 Hz, CH_2CH=CH_2), and 5.88 (1H, m, CH_2CH=CH_2). Found: C, 78.56; H, 11.91%. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98%.

The olefin (612 mg, 3.3 mmol) was oxidized with MCPBA (1.13 g, 5.0 mmol) in dichloromethane (20 ml) at room temperature for 17 h. The reaction mixture was worked up as usual and purified by chromatography to yield **14** (656 mg), bp 117—119 °C (14 Torr); MS, *m/e* 184 (M^+) and 166; IR, 3440, 1255, and 1015 cm^{-1}; NMR, δ 1.91 [2H, d, J=8 Hz, CH_2CH(-O-)CH_2], 2.49 and 2.81 [each 1H, dd, J=5, 2 and 5, 2 Hz, CH_2CH(-O-)CH_2], and 3.19 [1H, m, CH_2-CH(-O-)CH_2]. Found: C, 71.77; H, 10.89%. Calcd for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94%.

iii): 5-Nonanone (1.1 g) was reacted with allylmagnesium bromide, prepared from allyl bromide (2 g) and magnesuim (0.4 g) in ether, in the same manner as mentioned above to give 4-butyl-1-octen-4-ol (1.2 g), which was used for the next epoxidation without further purification. The alkenyl alcohol (1.2 g) was treated with MCPBA (2.4 g) in dichloromethane (60 ml) at room temperature for 15 h. The reaction mixture was worked up as usual and purified by chromatography to give **15** (637 mg), bp 128—131 °C (bath temp) (18 Torr); MS, *m/e* 182 ($M^+ - H_2O$); IR, 3445 and 1250 cm^{-1}; NMR, δ 0.88 [6H, br t, J=7 Hz, $(CH_2)_3CH_3$ and 8-H], 2.45 and 2.77 [each 1H, dd, J=6, 3 and 6, 6 Hz, CH_2CH(-O-)CH_2], 3.09 [1H, m, CH_2CH(-O-)CH_2]. Found: C, 71.80, 12.06%. Calcd for $C_{12}H_{24}O_2$: C, 71.95; H, 12.08%.

Reactions of 1b, 13, 14, and 15 under Aqueous Conditions. *i)*: A solution of **1b** (104 mg, 0.56 mmol) in DMSO (17.25 ml) and water (5.75 ml) was stirred with KOH (370 mg, 5.6 mmol) at room temperature for 10 min and then at 108 °C (bath temp) for 1.4 h under nitrogen, when the spot of **1b** had disappeared on TLC. The mixture was cooled, poured into ice–water, and extracted with ethyl acetate. The acetate solution was washed with water, dried and evaporated to leave an oily residue (114 mg), showing two spots on TLC, which was separated into two fractions by preparative TLC over silica gel (20×20 cm^2, 5 plates), a 1:1 mixture of benzene and ether being used as a solvent. A more mobile fraction gave 2-(1-hydroxy-1-methylethyl)-4,4-pentamethyleneoxetane (**2b**, 74 mg), bp 98—102 °C (10 Torr); MS, *m/e* 184 (M^+), 166, 99, and 98; IR ($CHCl_3$), 3580, 3460, 1020, and 990 cm^{-1}; NMR, δ 1.02 and 1.16 (each 3H, s, CH_3), 2.06 and 2.32 (each 1H, dd, J=10.5 and 8 Hz, 3-H). Found: C, 71.44; H, 10.82%. Calcd for $C_{11}H_{20}O_2$: C, 71.74; H, 10.87%. A less mobile fraction afforded 1-(1-hydroxycyclohexyl)-3-methyl-2,3-butanediol (**3b**, 10 mg), amorphous; MS, *m/e* 202 (M^+) and 184; IR ($CHCl_3$), 3440 cm^{-1}; NMR, δ 1.14 and 1.18 (each 3H, s, CH_3 at C-3 and 4-H), and 3.73 (1H, dd, J=10 and 4 Hz, 2-H),

ii): A solution of **13** (172 mg, 1 mmol) in DMSO (30 ml) and water (10 ml) was heated up to 140 °C for 75 min with KOH (690 mg, 10 mmol) under nitrogen with stirring. The reaction mixture was worked up as described before and purified by chromatography over silica gel (7 g) with benzene–ether. More mobile fractions eluted with benzene–ether (5:1) gave 2-hydroxymethyl-4,4-hexamethyleneoxetane (**16**, 43 mg), bp 131—135 °C (bath temp) (17 Torr); MS, *m/e* 170 (M^+) and 152; IR, 3400, 1044, 965, and 876 cm^{-1}; NMR, δ 2.19 and 2.36 (each 1H, d, J=12 Hz, 3-H), 3.52 and 3.72 (each 1H, dd, J=12 and 4 Hz, CH_2OH), and 4.60 (1H, m, 2-H:). Found: C, 70.39; H, 10.71%. Calcd for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66%. Less mobile fractions eluted with benzene–ether (1 : 1) afforded 4,4-hexamethylene-1,2,4-butanetriol (**19**, 103 mg), mp 69—72 °C (from hexane); MS, *m/e* 188 (M^+), 170, and 157; IR (Nujol), 3280 cm^{-1}; NMR δ 3.40 and 3.58 (each 1H, dd, J=11, 6 and 11, 4 Hz, 1-H), 3.52 and 4.49 (2H and 1H, each br s, OH), and 4.04 (1H, m, 2-H). Found: C, 63.56; H, 10.76%. Calcd for $C_{10}H_{20}O_3$: C, 63.79; H, 10.71%.

iii): Compound **14** (190 mg) in DMSO (30 ml) and water (10 ml) was heated up to 85 °C (bath temp) (at 50 °C for 0.5 h, at 80 °C for 0.5 h, and 85 °C for 0.5 h) with KOH (690 mg) in the same manner as mentioned above. The reaction mixture was worked up and purified as usual to give

2-hydroxymethyl-4,4-heptamethyleneoxetane (**17**, 38 mg), bp 142—144 °C (bath temp) (17 Torr), and 4,4-heptamethylene-1,2,4-butanetriol (**20**, 122 mg), mp 86—88 °C (from hexane). **17**, MS, *m/e* 184 (M^+) and 166; IR, 3390, 957, and 910 cm^{-1}; NMR, δ 2.22 (2H, d, J=8 Hz, 3-H), 3.64 (2H, dd, J=7 and 3 Hz, CH_2OH), and 4.66 (1H, m, 2-H). Found: C, 71.30; H, 11.04%. Calcd for $C_{11}H_{30}O_2$: C, 71.69; H, 10.94%. **20**, MS, *m/e* 202 (M^+) and 171; IR (Nujol), 3260 cm^{-1}; NMR, δ 3.44 and 3.57 (each 1H, dd, J=11, 6 and 11, 4 Hz, 1-H), and 4.06 (1H, m, 2-H). Found: C, 65.33; H, 11.00%. Calcd for $C_{11}H_{22}O_3$: C, 65.31; H, 10.96%.

iv): Compound **15** (202 mg) in DMSO (30 ml) and water (10 ml) was heated with KOH (690 mg) almost in the same manner (at 40 °C for 0.5 h, at 60 °C for 0.5 h, and at 80 °C for 0.25 h) as mentioned above, and the reaction mixture was worked up and purified as described before to give 4,4-dibutyl-2-hydroxymethyloxetane (**18**, 43 mg), bp 113—116 °C (bath temp) (17 Torr), and 4-butyl-1,2,4-octanetriol (**21**, 154 mg), amorphous. **18**, MS, *m/e* 200 (M^+), 182, and 143; IR, 3410, 965, and 928 cm^{-1}; NMR, δ 2.21 (2H, d, J=8 Hz, 3-H), 3.54 and 3.68 (each 1H, dd, J=12, 5 and 12, 3.5 Hz, CH_2OH), and 4.60 (1H, m, 2-H). Found: C, 71.58; H, 12.10%. Calcd for $C_{12}H_{24}O_2$: C, 71.95; H, 12.08%. **21** MS, *m/e* 218 (M^+) and 187; IR, 3360 cm^{-1}; NMR, δ 0.87 (6H, br t, J=7 Hz, CH_3), 2.95 and 4.25 (2H and 1H, each br s, OH), 3.40 and 3.56 (each 1H, dd, J=11.5, 7 and 11.5, 3.5 Hz, 1-H), and 4.03 (1H, m, 2-H). Found: C, 65.88; H, 12.30%. Calcd for $C_{12}H_{26}O_3$: C, 66.01; H, 12.00%.

Preparation of 1-(1,2-Epoxycyclopentyl)-, 1-(1,2-Epoxycyclohexyl)-, 1-(1,2-Epoxycycloheptyl)-, and 1-(1,2-Epoxycyclooctyl)-2-methyl-2-propanols (22—25). *i)*: A suspended mixture of cyclopentanone (8.4 g, 0.1 mol), cyanoacetic acid (8.5 g, 0.1 mol), and ammonium acetate (1.5 g, purity 95%) was refluxed in dry benzene (12 ml) on an oil-bath (145—155 °C) for 2 h under stirring, water being removed by a Dean-Stark apparatus.[7] The reaction mixture was evaporated to remove benzene, leaving yellow solid residue, which was submitted to distillation with concomitant decarboxylation at 155—165 °C (bath temp) under reduced pressure (40—55 Torr). Fractions distilled at 60—80 °C (40—55 Torr) were collected and dissolved in ether (25 ml), washed with 10% aq Na_2CO_3 and water, dried, evaporated and again distilled to give 2-(1-cyclopentenyl)acetonitrile (5.85 g), bp 68—71 °C (12 Torr); MS, *m/e* 107 (M^+); IR, 2240 and 1638 cm^{-1}; NMR, δ 3.14 (2H, s, 2-H) and 5.76 (1H, m, C=CH).

The nitrile (5.5 g) was stirred with 10% aq KOH (160 ml) on an oil bath (120—130 °C) for 4.5 h under nitrogen. The reaction mixture was cooled, washed with ether (50 ml), made acidic to pH ≈2 with 2M aq HCl, and extracted with chloroform (5×30 ml). The chloroform solution was dried and evaporated to give crude 2-(1-cyclopentenyl)acetic acid (5.79 g); IR (Nujol), 3040, 2640, and 1710 cm^{-1}; NMR, δ 3.18 (2H, s) and 5.60 (1H, br s). The crude acid was converted into the methyl ester as follows. To a solution of water (5 ml), ether (5 ml), and ethanol (35 ml) containing KOH (purity 85%) heated at 60—65 °C was added dropwise *p*-tolylsulfonylmethylnitrosamide (10.8 g) in ether (82 ml) under stirring, and the distilled diazomethane was dissolved in cold ether.[18] To the diazomethane solution cooled with an ice–salt bath was added dropwise the crude acid (2.0 g) in ether (14 ml), and the ether solution was evaporated to give crude methyl 2-(1-cyclopentenyl)acetate (2.3 g), which was used for the next reaction without further purification; IR, 1745 and 1655 cm^{-1}; NMR, δ 3.17 (2H, s), 3.72 (3H, s), and 5.62 (1H, m).

To lithium (6.6 g) in dry ether (252 ml) was added dropwise methyl iodide (29 ml, 64.9 g) in ether (50 ml) under gentle reflux with stirring, and the mixture was then refluxed for 2 h. The methyllithium solution (170 ml) was added to a cold solution of the crude acetate (2.0 g) in ether (80 ml), and the whole solution was stirred at 0 °C for 1 h. After addition of water (50 ml), the reaction mixture was separated into two layers, and the aqueous layer was extracted with ether (3× 50 ml). All the ether solutions were combined, washed with water, dried and evaporated to leave an oily residue, which was purified by chromatography over silica gel (70 g) to give 1-(1-cyclopentenyl)-2-methyl-2-propanol (1.22 g), bp 74—76 °C (bath temp) (12 Torr); MS, *m/e* 140 (M^+), 125, and 122; IR, 3380, 1645, and 1370 cm^{-1}; NMR, δ 1.22 (6H, s, CH_3 at C-2 and 3-H), 1.70 (1H, s, OH), 2.36 [6H, br, m, $(CH_2)_3$], and 5.50 (1H, t, J=5 Hz, CH=C). Found: C, 77.12; H, 11.61%. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50%.

The unsaturated alcohol (570 mg) was epoxidized with MCPBA (1.7 g) in dichloromethane (30 ml) at 0 °C for 3 h in the same manner as described before. The reaction mixture was worked up and purified as usual to give **22** (578 mg), bp 90—92 °C (12 Torr) (bath temp); IR, 3440, 1210, and 1115 cm^{-1}; NMR, δ 1.28 and 1.35 (each 3H, s, CH_3 at C-2 and 3-H), 1.97 (2H, s, 1-H), and 3.31 (1H, s, CH(–O–)C). Found: C, 69.27; H, 10.33%. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32%.

ii): 2-(1-Cyclohexenyl)acetonitrile, bp 96—98 °C (bath temp) (15 Torr), was prepared according to the reported procedure.[18] The nitrile (8.6 g) was refluxed (bath temp, 120—130 °C) with 10% aq KOH for 4.5 h under nitrogen with stirring. The reaction mixture was cooled and washed with ether (50 ml). The aqueous solution was acidified with 2 M aq HCl to pH ≈2, and extracted with chloroform (4×50 ml). The chloroform extracts were worked up as usual to give crude 2-(1-cyclohexenyl)acetic acid (10.3 g); IR, 3000 and 1713 cm^{-1}; NMR δ 1.65 and 2.07 (each 4H, m), 3.02 (2H, s), 5.64 (1H, m), and 10.70 (1H, br, W_H=30 Hz). The crude acid (2.0 g) was then converted with diazomethane in ether[18] into the corresponding crude methyl ester (2.3 g), which was used for the next reaction without further purification; IR, 1745 and 1645 cm^{-1}; NMR, δ 1.61 and 2.02 (each 4H, m), 2.97 (2H, s), 3.67 (3H, s), and 5.56 (1H, m).

To a solution of the crude ester (2.3 g) in dry ether (100 ml) cooled with an ice-bath was added a methyllithium solution in ether (100 ml) (1.5 M CH_3Li in ether) under stirring, and the mixture was stirred at room temperature for 1 h. After dropwise addition of water (50 ml), the mixture was separated into two layers, and the aqueous solution was extracted with ether (3×50 ml). All the ether solutions were combined, washed with water (2×50 ml), dried and evaporated to leave an amorphous residue, which was purified by chromatography to give 1-(1-cyclohexenyl)-2-methyl-2-propanol (1.16 g), bp 46—48 °C (bath temp) (0.15 Torr); MS, *m/e* 154 (M^+), 139, and 136; IR, 3400, 1660, and 1150 cm^{-1}; NMR, δ 1.01 (6H, s, CH_3 at C-2 and C-1), 1.62 [4H, CH_2-$(CH_2)_2CH_2$], 2.08 [4H, m, $CH_2(CH_2)_2CH_2$], 2.13 (2H, s, 3-H), and 5.52 (1H, br s, W_H=8 Hz, C=CH). Found: C, 77.49; H, 11.72%. Calcd for $C_{10}H_{18}O$: C, 77.86; H, 11.76%.

The unsaturated alcohol (505 mg) was oxidized with MCPBA (1.4 g) in chloroform (30 ml) at 0 °C for 5 h under stirring. The reaction mixture was worked up and purified as described above to give **23** (506 mg), bp 95—97 °C (bath temp) (15 Torr); MS, *m/e* 170 (M^+), 155, and 152; IR, 3440, 1380, 1370, and 1250 cm^{-1}; NMR, δ 1.27 and 1.37 (each 3H, s, CH_3 at C-2 and 3-H), 1.72 and 1.86 (each 1H, d, J=15 Hz, 1-H), and 3.06 [1H, t, J=2 Hz, $CH_2CH(–O–)$]. Found: C, 70.43; H, 10.58%. Calcd for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66%.

iii): Cycloheptenylacetonitrile (4.3 g), bp 98—100 °C (12

Torr), was prepared by treatment of cycloheptanone (5.6 g) with cyanoacetic acid (4.3 g) and ammonium acetate (1.0 g) in benzene (10 ml) at 165—175 °C (bath temp) for 2 h in almost the same manner as cyclopentylacetonitrile; IR, 2440 and 1615 cm^{-1}; NMR, δ 3.05 (2H, s) and 5.92 (1H, t, J=6 Hz). The acetonitrile (4.2 g) was then hydrolyzed by heating (120—130 °C) (bath temp) in 15% aq KOH (80 ml) for 16 h to yield the corresponding crude acid (3.54 g); IR, 3000, 2660, 1715, and 1630 cm^{-1}; NMR, δ 3.05 (2H, s) and 5.74 (1H, t, J=6 Hz). The crude acid (0.6 g) was converted into the methyl ester (0.64 g); IR, 1745 cm^{-1}; NMR, δ 3.02 (2H, s), 3.68 (3H, s), and 5.69 (1H, t, J=7 Hz). The crude methyl ester (0.62 g) was transformed by treatment with methyllithium, prepared from methyl iodide (15 g) and lithium (1.63 g) in ether (80 ml), at room temperature for 15 h into 1-(1-cycloheptenyl)-2-methyl-2-propanol (0.49 g), bp 88—91 °C (bath temp) (12 Torr); MS, *m/e* 168 (M^+), 153, and 150; IR, 3380 and 1370 cm^{-1}; NMR, δ 1.22 (6H, s), 2.20 (2H, s), and 5.68 (1H, t, J=8 Hz). Found: C, 78.33; H, 12.01%. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98%. The unsaturated alcohol (0.44 g) was oxidized with MCPBA (1.3 g) in chloroform (15 ml) at 0 °C for 4 h under stirring. The reaction mixture was worked up and purified as usual to give **24** (0.38 g), bp 105—107 °C (bath temp) (12 Torr); MS, *m/e* 169 ($M^+ - CH_3$) and 166 ($M^+ - H_2O$); IR, 3440, 1240, and 1150 cm^{-1}; NMR, δ 1.21 and 1.38 (each 3H, s), 1.79 (2H, s), and 2.99 (1H, dd, J=4 and 6 Hz). Found: C, 71.39; H, 10.87%. Calcd for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94%.

iv): Cyclooctanone (2.5 g) was refluxed with cyanoacetic acid (1.7 g) and ammonium acetate (0.3 g) in benzene (10 ml) at 170—180 °C (bath temp) for 2 h and then at 100 °C (bath temp) for 1 h under stirring. After removal of benzene, the mixture was gently heated to *ca.* 190 °C (bath temp) under reduced pressure (20—40 Torr) until evolution of carbon dioxide gas ceased, and was then distilled. Fractions boiling at 90—105 °C (15 Torr) were collected and dissolved in ethyl acetate (50 ml). The acetate solution was washed with 10% aq Na_2CO_3 (2×10 ml) and with water (10 ml), dried and evaporated to leave an oily residue, which was distilled fractionally to give 1-cyclooctenylacetonitrile (1.89 g), bp 103—105 °C (13 Torr); IR, 2240 cm^{-1}; NMR, δ 1.51 (8H, br s), 3.06 (2H, s), and 5.74 (1H, t, J=8 Hz).

The nitrile (2.1 g) was heated with 15% aq KOH (70 ml) at 120—130 °C (bath temp) for 11 h under nitrogen with stirring. After being shaken with ether (100 ml), the mixture was made acidic (pH ≈2) with 2 M aq HCl and extracted with dichloromethane (100 ml). The dichloromethane solution, after usual work-up, left crude cyclooctenylacetic acid (1.81 g); IR, 3000 and 1713 cm^{-1}; NMR, δ 1.50 (8H, s), 3.05 (2H, s), and 5.58 (1H, t, J=8 Hz). The crude acid (1.9 g) in ether (10 ml) was converted into the methyl ester (1.97 g), oily, by treatment with diazomethane, prepared from *p*-tolylsulfonylmethylnitrosamide (11 g), ethanol (15 ml), KOH (4 g), water (6 ml), and ether (6 ml);[18] IR, 1745 cm^{-1}; NMR, δ 1.49 (8H, s), 3.04 (2H, s), 3.70 (3H, s), and 5.56 (1H, t, J=8 Hz). To the crude methyl ester (1.0 g) in ether (20 ml) was added dropwise a methyllithium solution in ether (1.5 M, 110 ml) at ice–water bath temperature under stirring during 0.5 h. The mixture was stirred at the temperature and mixed with ice–water (30 ml). The whole reaction mixture was poured into saturated brine and extracted with ether (3×50 ml). The ether solution was worked up and purified by chromatography over silica gel (30 g) as mentioned above to give 1-(1-cyclooctenyl)-2-methyl-2-propanol (0.78 g), bp 113—115 °C (bath temp) (12 Torr); MS, *m/e* 182 (M^+), 167, and 164; IR, 3420 cm^{-1}; NMR, δ 1.13 (6H, s), 1.45 (8H, s) and 5.40 (1H, t, J=8 Hz). Found: C, 79.14; H, 12.08%. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16%.

The unsaturated alcohol (620 mg) in dichloromethane (22 ml) was oxidized with MCPBA (1.73 g) at 0 °C under stirring for 2.5 h. The reaction was ceased by addition of 5% aq $Na_2S_2O_3$ (5 ml) and the mixture was worked up as usual and purified by chromatography over silica gel (20 g). Fractions eluted with benzene and benzene–ether (10 : 1) gave **25** (411 mg), bp 125—127 °C (bath temp) (12 Torr), showing a single spot on TLC; MS, *m/e* 198 (M^+), 183, and 180; IR, 3460 and 1260 cm^{-1}; NMR, δ 1.24 and 1.39 (each 3H, s) and 2.80 (1H, dd, J=4 and 8 Hz). Found: C, 72.40; H, 11.05%. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18%.

Reactions of 22, 23, 24, and 25 under Aqueous Conditions.

i): A solution of **22** (156 mg) in DMSO (30 ml) was heated with KOH (680 mg, 85% purity) in water (10 ml) at 130 °C (bath temp) for 0.5 h and then at 135 °C (bath temp) for 1 h under nitrogen with stirring. The reaction mixture was cooled, poured into brine, and extracted with ethyl acetate (6×50 ml). The acetate solution was washed with saturated brine (2×50 ml), dried and evaporated to leave an oily residue (320 mg), which was separated by chromatography over silica gel (8 g) with benzene–ether (5: 1). Most mobile fractions gave 2,2-(2-hydroxytetramethylene)-4,4-dimethyloxetane (**26**, 55 mg), bp 85—87 °C (bath temp) (12 Torr); MS, *m/e* 156 (M^+), 141, and 138; IR, 3420, 970, 950, and 930 cm^{-1}; NMR, δ 1.42 and 1.46 (each 3H, s, C<u>H</u>$_3$ at C-4), 2.13 and 2.67 (each 1H, ABq, J=11 Hz, 3-<u>H</u>), and 4.02 [1H, t, J=4 Hz, C<u>H</u>(OH)]. Found: C, 68.92; H, 10.35%. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32%. Compound **26** (16 mg) was converted by treatment with acetic anhydride (0.3 ml) and pyridine (0.6 ml) at 20 °C for 16 h into the monoacetate (**26a**), oily; MS, *m/e* 198 (M^+), 183, and 138; IR, 1745 and 850 cm^{-1}; NMR, δ 1.42 (6H, s), 2.07 (3H, s), 2.20 and 2.54 (each 1H, ABq, J=12 Hz), and 5.16 (1H, m).

Middle fractions afforded 2-(2-hydroxy-2-methylpropyl)-2-cyclopenten-1-ol (**31**, 13 mg), bp 81—83 °C (bath temp) (15 Torr); MS, *m/e* 141 ($M^+ - CH_3$) and 138 ($M^+ - H_2O$); IR, 3280, 1115, and 840 cm^{-1}; NMR, δ 1.22 and 1.30 (each 3H, s, C<u>H</u>$_3$ at C-2 and 3-<u>H</u>), 3.73 (2H, br, W_H=16 Hz, O<u>H</u>), 4.68 (1H, m, 1-<u>H</u>), and 5.83 (1H, br s, 3-<u>H</u>). Found: C, 68.83; H, 10.46%. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32%. The glycol (**31**, 10 mg) was converted into the monoacetate (**31a**, 10 mg), oily; MS, *m/e* 183 ($M^+ - CH_3$), 180, and 138; IR, 3440, 1735, 1120, and 855 cm^{-1}; NMR, δ 1.20 and 1.24 (each 3H, s), 2.05 (3H, s), 5.74 (1H, m), and 5.84 (1H, br s).

Least mobile fractions gave 1-(2-hydroxy-2-methylpropyl)-cyclopentane-1,2-diol (30 mg), mp 71—73 °C (from hexane); MS, *m/e* 174 (M^+), 159, and 156; IR ($CHCl_3$), 3620 and 3400 cm^{-1}; NMR, δ 1.35 and 1.43 (each 3H, s, C<u>H</u>$_3$ at C-2 and 3-<u>H</u>), 2.91 (3H, br, W_H=8 Hz, O<u>H</u>), and 4.03 (1H, m, 2-<u>H</u>). Found: C, 62.41; H, 10.44%. Calcd for $C_9H_{16}O_3$: C, 62.04; H, 10.41%. The triol (16 mg) gave the monoacetate (18 mg), amorphous; MS, *m/e* 190 (M^+), 175, 172, and 130; IR (Nujol), 3280 and 1735 cm^{-1}; NMR, δ 1.24 and 1.36 (each 3H, s), 1.86 (2H, s), 2.06 (3H, s), and 5.00 (1H, dd, J=5 and 1 Hz).

ii): Compound **23** (170 mg) in DMSO (30 ml) was heated with KOH (685 mg, purity 85%) in water (10 ml) at *ca.* 140 °C for 1.5 h under nitrogen with stirring. The reaction mixture was worked up as described above and separated into three fractions by chromatography over silica gel (7 g), a 5 : 1 mixture of benzene and ether being used as solvent. The most mobile fraction gave 2,2-(2-hydroxypentamethylene)-4,4-dimethyloxetane (**27**, 78 mg), bp 83—85 °C (bath temp) (12 Torr); MS, *m/e* 170 (M^+), 155, and 152; IR, 3420, 967, and 880 cm^{-1}; NMR, δ 1.40 and 1.47 (each 3H, s, C<u>H</u>$_3$

at C-4), 1.88 and 2.40 (each 1H, d, J=11 Hz, 3-H), and 3.36 [1H, dd, J=11 and 4 Hz, CH(OH)]. Found: C, 70.63; H, 10.71%. Calcd for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66%. Compound **27** (15.5 mg) was converted into the monoacetate (**27a**, 15 mg), oily; MS, 212 (M^+); IR, 1745, 970, and 880 cm^{-1}; NMR, δ 1.40 and 1.44 (each 3H, s), 2.13 (3H, s), 1.99 and 2.30 (each 1H, d, J=10 Hz), and 4.72 (1H, dd, J=10 and 4 Hz).

The middle fraction afforded 2,2-dimethyl-1-oxaperhydroinden-3a-ol (**29**, 12 mg), mp 69—71 °C (from hexane); MS, *m/e* 170 (M^+), 155, and 137; IR ($CHCl_3$), 3600, 3420, 1150, and 1105 cm^{-1}; NMR, δ 1.35 (6H, s, CH_3 at C-2), 1.84 and 1.94 (each 1H, ABq, J=13 Hz, 3-H), and 3.79 (1H, t, J=4 Hz, 7a-H). Found: C, 70.22; H, 10.69%. Calcd for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66%. The least mobile fraction gave 1-(2-hydroxy-2-methylpropyl)cyclohexane-1,2-diol (22 mg), amorphous; MS, *m/e* 188 (M^+), 173, and 170; IR (Nujol), 3360 cm^{-1}; NMR, δ 1.28 and 1.38 (each 3H, s, CH_3 at C-2 and 3-H), 3.20 (3H, br, OH), and 3.46 (1H, dd, J=8 and 4 Hz, 2-H). Found: C, 63.51; H, 10.75%. Calcd for $C_{10}H_{20}O_3$: C, 63.79; H, 10.71%. The triol (15 mg) afforded the monoacetate (16 mg), amorphous; MS, *m/e* 215 ($M^+ - CH_3$) and 212 ($M^+ - H_2O$); IR, 3410 and 1737 cm^{-1}; NMR, δ 1.28 and 1.34 (each 3H, s), 2.07 (3H, s), and 4.75 (1H, dd, J=8 and 4 Hz).

iii): Compound **24** (186 mg) was heated at *ca.* 115 °C (bath temp) for 2 h with KOH (685 mg, purity 85%) in DMSO (30 ml) and water (10 ml) under nitrogen with stirring. The reaction mixture was worked up as usual and separated by chromatography over silica gel (6 g) with benzene–ether (10: 1) to yield the unchanged starting material (**24**, 25 mg) and the following three products: 4,4-(2-hydroxyhexamethylene)-2,2-dimethyloxetane (**28**, 39 mg), 2,2-dimethyl-1-oxaperhydroazulen-3a-ol (**30**, 36 mg), and 2-(2-hydroxy-2-methylpropyl)-2-cyclohepten-1-ol (**32**, 15 mg), **28**, bp 109—112 °C (bath temp) (12 Torr); MS, 184 (M^+), 169, and 151; IR ($CHCl_3$), 3600, 3440, 988, and 955 cm^{-1}; NMR, δ 1.36 and 1.47 (each 3H, s, CH_3 at C-2), 1.96 and 2.52 (each 1H, d, J=12 Hz, 3-H), and 3.41 [1H, J=10 and 4 Hz, CH(OH)]. Found: C, 71.37; H, 11.00%. Calcd for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94%. Monoacetate (**28a**) of **28**, oily, MS, *m/e* 226 (M^+), 211, 208, and 166; IR, 1740, 1040, and 850 cm^{-1}; NMR, δ 1.24 and 1.42 (each 3H, s), 2.10 (3H, s), 2.29 (1H, d, J=12 Hz), and 4.19 (1H, dd, J=10 and 4 Hz). **30**, mp 60—62 °C (from hexane); MS, *m/e* 184 (M^+), 169, and 166; IR ($CHCl_3$), 3600, 3440, 1105, and 1070 cm^{-1}; NMR, δ 1.28 and 1.39 (each 3H, s, CH_3 at C-2), 1.82 and 1.91 (each 1H, d, J=12 Hz, 3-H), and 3.96 (1H, dd, J=9 and 3 Hz). Found: C, 71.46; H, 10.98%. Calcd for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94%. **32**, mp 76—78 °C (from hexane); MS, 169 ($M^+ - CH_3$) and 166 ($M^+ - H_2O$); IR ($CHCl_3$), 3620 and 3400 cm^{-1}; NMR, δ 1.20 and 1.22 (each 3H, s, CH_3 at C-2 and 3-H), 2.24 and 2.36 (each 1H, ABq, J=14 Hz, 1-H), 4.40 [1H, dd, J=6 and 2 Hz, CH(OH)], and 5.56 (1H, t, J=7 Hz, 3-H). Found: C, 71.32; H, 10.69%. Calcd for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94%.

iv): Compound **25** (198 mg) was heated at *ca.* 140 °C (bath temp) for 2.5 h with KOH (685 mg, purity 85%) in DMSO (30 ml) and water (10 ml) under nitrogen with stirring. The reaction mixture was worked up as mentioned above and purified by chromatography as usual to give the starting material (**25**, 170 mg) unchanged.

Hydrolysis of Cycloalkene Oxides (33—36). Each (112—182 mg) of compounds **33**,[19] **34**,[20] **35**,[21] and **36**[22] in DMSO (15 ml) was added rapidly to an aqueous KOH (10 mol equiv) solution (5 ml) heated at 100—110 °C (bath temp), and the whole solution was stirred at the temperature for 0.5 h or for 3 h. After being cooled, the mixture was worked up as usual to give the hydrolysis product (**37**[23] or **38**[24]) and/or the starting epoxides. The result is summarized in the text.

*Reactions of **1b** and **15** under Anhydrous Conditions.* *i)*: A suspension of **1b** (186 mg, 1 mmol) and sodium hydride (NaH, 120 mg, purity 50%, 2.5 mmol) in dry THF (30 ml) was heated gently under reflux for 11 h. The reaction mixture was cooled, poured into ice–water, and extracted with ethyl acetate. The acetate solution was worked up as usual to leave an oily residue (170 mg), showing two spots, which was separated into two fractions by preparative TLC (5 plates) over silica gel. The less mobile fraction gave **2b** (53 mg) and and the more mobile the starting epoxide (**1b**, 102 mg).

ii): A suspended mixture of **15** (100 mg, 0.5 mmol) and NaH (60 mg, purity 50%, 1.25 mmol) in THF (10 ml) was refluxed for 13 h under nitrogen. The reaction mixture was worked up as mentioned above and purified by chromatography over silica gel (6 g) with benzene–ether (2: 1) to yield the starting epoxide (**15**, 17 mg) and 4,4-dibutyl-2-(4-butyl-2,4-dihydroxyoctyloxy)oxolane (**4a**, 64 mg), amorphous; MS, *m/e* 400 (M^+), 382, and 364; IR (Nujol), 3460, 1135, and 1070 cm^{-1}; NMR, δ 0.90 (12H, br t, J=7 Hz, CH_3), 3.48 [4H, m, CH_2(–O–)], 3.64 [1H, m, CH(OH)], and 4.21 [1H, m, CH(–O–)]. Found: C, 71.63; H, 12.10%. Calcd for $C_{24}H_{48}O_4$: C, 71.95; H, 12.10%.

*Reactions of **23**, **24**, and **25** under Anhydrous Conditions.* *i)*: A solution of **23** (120 mg) in THF (10 ml) was added to a stirred suspension of mineral-oil free NaH (85 mg) in THF (10 ml). The mixture was refluxed gently for 15 h, cooled and mixed with water (2 ml). After removal of THF by evaporation, the mixture was poured into brine and extracted with ethyl acetate, dried and evaporated to leave oily residue (125 mg), which was separated by column chromatography over silica gel (4 g) with benzene–ether (2: 1) and subsequent preparative TLC to yield three products, 2-methylenecyclohexanol (**39**, 38 mg), oxetane **27** (33 mg), and 2-(2-hydroxy-2-methylpropyl)-2-cyclohexen-1-ol (**40**, 12 mg). **29**, bp 65—67 °C (bath temp) (12 Torr); MS, *m/e* 112 (M^+) and 94; IR, 3340, 3080, 1640, and 897 cm^{-1}; NMR, δ 4.07 (1H, m, 1-H), 4.73 and 4.86 (each 1H, s, $=CH_2$). Found: C, 74.61; H, 10.83%. Calcd for $C_7H_{12}O$: C, 74.95; H, 10.78%. **40**, bp 97—98 °C (bath temp) (12 Torr); MS, *m/e* 170 (M^+), 155, and 152; IR, 3300 cm^{-1}; NMR, δ 1.21 and 1.28 (each 3H, CH_3 at C-2 and 3-H), 3.72 (2H, br, OH), 4.10 and 5.56 (each 1H, t, J=4 Hz, 1- and 3-H). Found: C, 70.18; H, 10.71%. $C_{10}H_{18}O_2$: C, 70.54; H, 10.66%.

ii): A suspension of **24** (170 mg) in dry THF (20 ml) containing NaH (110 mg) was heated under reflux for 15 h. The mixture was worked up as mentioned above and separated by column chromatography over silica gel (6 g) with benzene–ether (10: 1) to yield the unchanged epoxide (**24**, 17 mg) and 2-methylenecycloheptanol (**41**, 69 mg), bp 73—76 °C (bath temp) (12 Torr); MS, *m/e* 126 (M^+) and 108; IR, 3360, 3060, 1645, and 895 cm^{-1}; NMR, δ 4.28 (1H, t, J=6 Hz, 1-H), 4.88 (1H, s, $C=CH_2$), and 5.00 (1H, t, J=1.5 Hz, $C=CH_2$). Found: C, 75.83; H, 11.30%. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18%.

iii): Compound **25** (199 mg) was treated with NaH (130 mg) in THF (20 ml) in the same manner as **24**. The reaction mixture was worked up as mentioned above and separated by chromatography over silica gel (5.5 g) with benzene–ether (10 : 1), giving the starting epoxide (**25**, 103 mg) and 2-methylenecyclooctanol (**42**, 26 mg): **42**, bp 92—95 °C (12 Torr); MS, *m/e* 140 (M^+) and 122; IR, 3400, 3060, 1630, and 895 cm^{-1}; NMR, δ 4.19 (1H, dd, J=8 and 6 Hz, 1-H), 4.96 and 5.12 (each 1H, s, $C=CH_2$). Found: C, 76.87; H, 11.56%. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50%.

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